AMENDMENTS TO THE SPECIFICATION

On page 1, line 2, please add the following paragraph below:

The present application is a U.S. National Stage Application of PCT/JP2004/011293 (WO 2005/012272), filed July 30, 2004, which in turn claimed the prior benefit of Japanese patent application JP 2003-285341, filed August 1, 2003, each of which is incorporated herein by reference in its entirety.

On page 6, please delete the paragraph beginning on line 13 and ending on line 18, and replace it with the following.

-- (13) 3-(2-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3-oxazol-5-yl)propionic acid, 2-(2-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-isobutyl-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3-oxazol-5-yl)acetic acid, or a salt thereof; --

Please delete the paragraph beginning on page 22, line 18, and ending on page 23, line 15, and replace it with the following.

-- The compound represented by the formula [1] includes, particularly preferably, 3-(2-{3-[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]propyl}-1,3-thiazol-5-yl)propionic acid, 3-(2-{2-[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]ethyl}-1,3-thiazol-4-yl)propionic acid, 3-(2-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3-oxazol-5-yl)propionic acid, 2-(2-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-isobutyl-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3-oxazol-5-yl)acetic acid, 5-(3-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,2,4-oxadiazol-5-yl)pentanoic acid, 5-(3-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,2,4-oxadiazol-5-yl)pentanoic acid, 5-(3-{[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-

dimethoxyphenyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,2,4-oxodiazol-5-yl)pentanoic acid and the like. --

On page 128, please delete the paragraph beginning on line 10 and ending on line 12, and replace it with the following.

-- 3-(2-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3-oxazol-5-yl)propionic acid --

On page 129, please delete the paragraph beginning on line 1 and ending on line 5, and replace it with the following.

-- (1) According to a similar manner to that of Example 27-(1), methyl 3-(2-{[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3-oxazol-5-yl)propionate was obtained. --

On page 133, please delete the paragraph beginning on line 15 and ending on line 17, and replace it with the following.

-- 2-(2-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-isobutyl-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3-oxazol-5-yl)acetic acid --

Please delete the paragraph beginning on page 164, line 9, and ending on page 165, line 4, and replace it with the following.

-- (1) A solution of ethyl 3-(2-{[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]acetyl}hydrazino))-3-oxopropionate (1.0 g) obtained in Example 55-(1) and Lawesson's reagent (0.96 g) in THF (50 ml) was stirred at 80°C for 1 hour. The reaction solution was poured into water, followed by extraction with ethyl acetate. This extract was washed with an aqueous saturated sodium chloride solution, dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to obtain ethyl [[5-(2-]] 2-(5-{[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-1,2,3,5-tetrahydro-2-oxo-4,1-benzoxazepin-3-yl]methyl}-1,3,4-thiadiazol-2-yl)acetate (0.8 g) as a white amorphous crystal. --

Please delete the paragraph beginning on page 165, line 12, and ending on page 166, line 2, and replace it with the following.

-- (2) A mixture of ethyl [[5-(2-]] 2-(5-{[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-1,2,3,5-tetrahydro-2-oxo-4,1-benzoxazepin-3-yl]methyl}-1,3,4-thiadiazol-2-yl)acetate (0.9 g) obtained in Example 56-(1), a 1N aqueous saturated sodium hydroxide solution (8.0 ml) and methanol (20 ml) was stirred at room temperature for 30 minutes. This mixture was diluted with water (50 ml), acidified, and extracted with chloroform (50 ml) twice. This extract was washed with an aqueous saturated sodium chloride solution, dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to obtain [[ethyl 5-(2-]] 2-(5-{[(3R,5S)-1-(3-~~acetoxy~~hydroxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-1,2,3,5-tetrahydro-2-oxo-4,1-benzoxazepin-3-yl]methyl}-1,3,4-thiadiazol-2-yl)~~acetate~~ acetic acid (0.19 g) as a white crystal. --

Please delete the paragraph beginning on page 166, line 15, and ending on page 167, line 14, and replace it with the following.

-- (1) Pivaloyl chloride (2.8 ml) was added to a solution of 2-[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]acetic acid (10 g) and triethylamine (3.2 ml) in THF (100 ml) at 0°C and the mixture was stirred at 0°C for 30 minutes. to the reaction solution at 0°C, ethyl 4-hydrazino-4-oxobutanoate (3.7 g) was added and triethylamine (3.2 ml) was then added dropwise. After stirring at room temperature for 2 hours, the reaction solution was diluted with ethyl acetate (50 ml). This diluted solution was washed with 0.1N hydrochloric acid, a 5% aqueous potassium hydrogen sulfate solution, an aqueous saturated sodium hydrogen carbonate solution and an aqueous saturated sodium chloride solution, dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to obtain ethyl 4-[[({2-[]] (2-{[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-1,2,3,5-tetrahydro-2-oxo-4,1-benzoxazepin-3-yl]acetyl}hydrazino)-4-oxobutanoate (3.6 g) as a colorless oil. --

Please delete the paragraph beginning on page 288, line 19, and ending on page 289, line 10, and replace it with the following.

-- (5) A 2N aqueous sodium hydroxide solution (2.60 ml, 5.20 mmol) was added to a solution of methyl 5-(3-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,2,4-oxadiazol-5-yl)pentanoate (1.04 g, 1.73 mmol) obtained in Example 136-(4) in ethanol (10 ml) and the mixture was stirred for 13 hours. The reaction solution was diluted with water and then washed with diethyl ether. The extract solution was acidified with 6N aqueous hydrochloric acid, extracted with ethyl acetate, washed with an aqueous saturated sodium chloride solution, dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography to obtain [[3-]] 5-(3-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(~~3-hydroxy-~~2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,2,4-oxadiazol-5-yl)pentanoic acid (0.89 g). --

Please delete the paragraph beginning on page 313, line 8, and ending on page 314, line 8, and replace it with the following.

-- (1) Triethylamine (1.2 ml, 8.5 mmol) and methyl 6-chloro-6-oxohexanoate (0.98 g, 5.5 mmol) were added dropwise to a solution of 3-[(3R,5S)-3-[(2Z)-2-amino-2-(hydroxyimino)ethyl]-7-chloro-5-(2,3-dimethoxyphenyl)-2-oxo-2,3-dihydro-4,1-benzoxazepin-1(5H)-yl]-2,2-dimethylpropyl acetate (2.67 g, 5.0 mmol) obtained in Example 58-(1) in THF (25 ml) under ice-cooling, and the mixture was stirred under ice-cooling for 40 minutes and then at room temperature for 1.5 hours. The reaction solution was concentrated under reduced pressure, water (25 ml) was added, and the mixture was heated to reflux for 18 hours. The reaction solution was extracted with ethyl acetate, washed with water and an aqueous saturated sodium chloride solution, and dried over magnesium sulfate. After concentration under reduced pressure, the residue was purified by silica gel column chromatography to obtain methyl [[3-]] 5-(3-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,2,4-oxodiazol-5-yl)pentanoate (1.73 g). --

Please delete the paragraph beginning on page 314, line 18, and ending on page 315, line 10, and replace it with the following.

-- (2) A 2N aqueous sodium hydroxide solution (5.25 ml, 10.5 mmol) was added to a solution of methyl [[3-]] 5-(3-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,2,4-oxodiazol-5-yl)pentanoate (1.73 g, 2.63 mmol) obtained in Example 154-(1) in ethanol (17 ml), and the mixture was stirred for 2 hours. The reaction solution was diluted with water and then washed with diethyl ether. The extract was acidified with 6N aqueous hydrochloric acid, extracted with ethyl acetate, washed with an aqueous saturated sodium chloride solution, dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography and then recrystallized from ethyl acetate-hexane to obtain [[3-]] 5-(3-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}1,2,4-oxadiazol-5-yl)pentanoic acid (1.06 g). --

Please delete the paragraph beginning on page 330, line 2, and ending on page 331, line 2, and replace it with the following.

-- (1) Pyridine (0.067 ml, 0.83 mmol) and trifluoromethanesulfonic acid anhydride (0.13 ml, 0.79 mmol) were added to a solution of ethyl (4S)-4-[[({2-]] (2-{[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-1,2,3,5-tetrahydro-2-oxo-4,1-benzoxazepin-3-yl]acetyl}hydrazino)-4-oxobutanoate (0.25 g, 0.38 mmol) obtained in Example 57-(1) in dichloromethane (4 ml) at -10°C, and the mixture was stirred for 1 hour. After further stirring at 0°C for 1 hour, an aqueous saturated sodium hydrogen carbonate solution (5 ml) was added thereto and the mixture was extracted with dichloromethane (80 ml). The organic layer was washed with water and an aqueous saturated sodium chloride solution, dried over magnesium sulfate, and then concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography [developing solvent: hexane-ethyl acetate (3:2)] to obtain ethyl 3-(5-{[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3,4-oxadiazol-2-yl)propionate (0.16 g, 0.25 mmol, 66%) as colorless noncrystalline powder. --

Please delete the paragraph beginning on page 331, line 13, and ending on page 332, line 5, and replace it with the following.

-- (2) A mixture of ethyl 3-(5-{[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3,4-oxadiazol-2-yl)propionate (0.1 g, 0.16 mmol) obtained in Example 163-(1), a 1N aqueous sodium hydroxide solution (0.6 ml) and ethanol (5 ml) was stirred at room temperature for 2 hours. The reaction solution was concentrated under reduced pressure, diluted with water (50 ml), and washed with diethyl ether (10 ml). The aqueous layer was acidified with 1N aqueous hydrochloric acid (1 ml) and then extracted with ethyl acetate (35 ml). The organic layer was washed with an aqueous saturated sodium chloride solution, dried over magnesium sulfate and then concentrated under reduced pressure to obtain 3-(5-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3,4-oxadiazol-2-yl)propionic acid (67 mg, 0.12 mmol, 75%) as a white crystal. --

On page 338, please delete the paragraph beginning on line 5 and ending on line 7, and replace it with the following.

-- (1) [[(2E)-]] 3-(4-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethyl propyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]acetyl}phenyl)propionic acid --

On page 340, please delete the paragraph beginning on line 12 and ending on line 14, and replace it with the following.

-- (1) [[(2E)-]] 3-(4-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethyl propyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]acetyl}phenyl)propionic acid --

On page 342, please delete the paragraph beginning on line 19 and ending on line 21, and replace it with the following.

--(1) [[(2E)-]] 3-(4-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethyl propyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]acetyl}phenyl)propionic acid –